A Hypothesis-Free Sensor Array Discriminates Whiskies for Brand, Age, and Taste

Han, Jinsong; Ma, Chao; Wang, Benhua; Bender, Markus; Bojanowski, Maximilian; Hergert, Marcel; Seehafer, Kai; Herrmann, Andreas; Bunz, Uwe H. F.

Published in:
Chem

DOI:
10.1016/j.chempr.2017.04.008

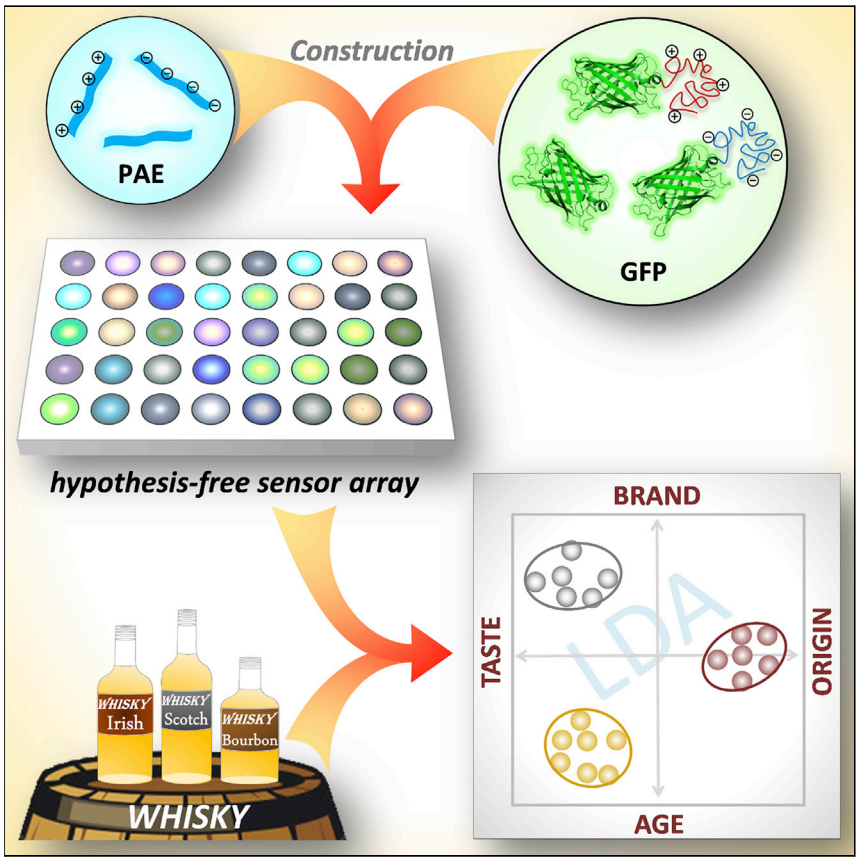
Publication date:
2017

Chem

CellPress

Article

A Hypothesis-Free Sensor Array Discriminates Whiskies for Brand, Age, and Taste



We apply two three-element arrays consisting either of different GFPs or of charged fluorescent poly(*p*-aryleneethynylene)s as a successful, hypothesis-free tongue that discriminates more than 30 whiskies according to their country of origin, brand, blend status, and taste. The underlying mechanism is the modulation of the fluorescence intensity of the elements of the sensor array by the different whiskies. Age, country of origin, blend status, and elements of taste were discriminated by the two very different tongues.

Jinsong Han, Chao Ma, Benhua Wang, ..., Kai Seehafer, Andreas Herrmann, Uwe H.F. Bunz

a.herrmann@rug.nl (A.H.)
uwe.bunz@oci.uni-heidelberg.de (U.H.F.B.)

HIGHLIGHTS

Two hypothesis-free sensor arrays discriminate whiskies on the basis of fluorescence modulation

The arrays recognize brand, origin, blending state, age, and taste of the tested whiskies

Non-specific interactions, such as hydrophobics and electrostatics, are operative

Han et al., Chem *2*, 817–824
June 8, 2017
http://dx.doi.org/10.1016/j.chempr.2017.04.008

Chem

CellPress

Article

A Hypothesis-Free Sensor Array Discriminates Whiskies for Brand, Age, and Taste

Jinsong Han,[1] Chao Ma,[3] Benhua Wang,[1] Markus Bender,[1] Maximilian Bojanowski,[1] Marcel Hergert,[1] Kai Seehafer,[1] Andreas Herrmann,[3,*] and Uwe H.F. Bunz[1,2,4,*]

SUMMARY

In biology, non-specific interactions are ubiquitous and important, whereas in chemistry, non-specificity or non-selectivity is suspect. We present simple tongues consisting of fluorescent polyelectrolytes or chimeric green fluorescent proteins (GFPs) to discriminating 33 different whiskies according to their country of origin (Ireland, US, or Scotland), brand, blend status (blend or single malt), age, and taste (rich or light). The mechanism of action for these tongues is differential quenching of the fluorescence of the poly(aryleneethynylene)s or the GFPs by the complex mixture of colorants (vanillin, vanillic acid, oak lactones, tannins, etc.; the interactome) extracted from the oak barrels and added caramel coloring. The differential binding and signal generation of the interactomes to the polymers and proteins result from hydrophobic and electrostatic interactions. The collected quenching data, i.e., the response patterns, were analyzed by linear discriminant analysis. Our tongues do not need any sample preparation and are equal or superior to state-of-the-art mass spectrometric methods with respect to speed, resolution, and efficiency of discrimination.

INTRODUCTION

Whisky was first produced in Scotland, where the oldest distillery was licensed in 1775. Since then, Scotch (and other whiskies) have been popular; the demand for expensive, specialized varieties has increased during the last decades. Today, countless whiskies of different origin, age, brand, blend status, taste, and price range are available. For high-end whiskies, asking prices range from €10,000 to €135,000 per bottle. For this type of price, one might worry about counterfeits, but that could also apply at the low end of the quality spectrum, where large amounts of cheap alcoholic beverages and low-quality counterfeits are sold as branded Scotch. Because it is difficult to obtain bona fide counterfeit whiskies, discriminating different whisky brands and sub-brands is a closely related and perhaps even more challenging and important task. We demonstrate discrimination of any whisky with ease by employing a hypothesis-free ad hoc tongue based on conjugated fluorescent polyelectrolytes or green fluorescent proteins (GFPs) fused to supercharged polypeptide chains.

A whisky sensor based on a dye-replacement assay has been reported by Anslyn et al.[1] The age of different whiskies was determined by detection of the concentration of gallate and other phenolic species, the concentration of which increases with age. However, the most common way to discriminate whiskies is to use mass spectrometry,[2–4] but simple quantitative UV-visible (UV-vis)[5] or mid-infrared (IR)

The Bigger Picture

The simple discrimination of complex analytes (beverages, foodstuffs, prescription drugs, etc.) is important for economic and health-related reasons. Because one cannot construct specific sensors or assays for analytes such as whiskies, powerful alternative methods are needed. Two hypothesis-free three-element arrays of charged fluorescent dyes (one composed of fluorescent proteins and the other composed of large π systems) differentiate more than 30 whiskies according to their differential fluorescence intensity modulation along the axes of age, area of origin, and taste. Small, arbitrarily selected arrays display a fundamentally important and unexpected power of discrimination for very different analytes, which we will harness in the future to discriminate counterfeit consumer goods (e.g., perfumes and alcoholic beverages) and prescription drugs (outdated, adulterated, counterfeit, brand free, etc.). Such an extension has a direct significant impact on society and some impact on the economy.

spectroscopy[6] have also been used with reasonable success, but with less than spectacular discriminative power.

Optoelectronic noses and tongues discriminate complex analytes and were popularized by Suslick et al.[7–9] and Anslyn et al.[10–12] More groups have now started working in this area.[13–18] The concepts of the two pioneers to construct functional sensor arrays differ. Whereas Suslick et al. state that chemical diversity is necessary in their tongues,[7] Anslyn et al. supported the idea that a relaxed lock-and-key principle is a powerful concept for creating sensor arrays for the discrimination of complex analytes.[11] Both concepts formulate sufficient but not necessary requisites for the construction of optoelectronic arrays. Rotello et al.[15,19] proposed that, for certain arrays, the structural prerequisites can be much more relaxed, favoring a concept of hypothesis-free sensor arrays.

A hypothesis-free sensor array would fundamentally allow us to sense "everything" with any fluorescent dye. Conjugated polyelectrolytes could represent such hypothesis-free arrays; they discriminate white wines,[20] fruit juices,[21] non-steroidal anti-inflammatory drugs,[22] and proteins[23] with small selected sensor arrays on the basis of fluorescence modulation, i.e., either quenching or fluorescence enhancement. The excited state of conjugated polymers lives for about 0.5–1 ns and is exquisitely sensitive to environmental change, be it solvent or any type of analyte that interacts either via hydrophobic or electrostatic interactions or via other forces. The magnitude of the effect that the analyte has on the fluorescence intensity is not predictable. A sensor array's fluorescence response to complex analytes such as whiskies can neither be predicted nor modeled because of the large interactome. If the complex analyte is colored (as with whisky), differential quenching of all of the sensor elements' fluorescence is observed. Here, we exploit arrays to discriminate whiskies according to their region of origin, brand, age, and taste.

RESULTS

Table 1 (Figures S1 and S2) shows the whiskies selected for study. A library of 22 poly(*p*-aryleneethynylene)s (PAEs; for the structures, see Figure S3) was available. Of these, nine are positively charged, four are neutral, and nine are negatively charged. We checked all of them against a sub-section of the tested whiskies (Table 1) by using a plate reader. From the recorded fluorescence response patterns, we concluded that positively charged PAEs (0.3 mL, 2 μM) give an optical signal with 3 μL of whisky, whereas for neutral PAEs and for negatively charged PAEs, we need 30 and 60 μL, respectively, of the whiskies to elicit a similar fluorescence response (see Figures S7, S8, and S10). Although there is significant selectivity and cross-reactivity for the whiskies for all of the different PAEs, the positively charged PAEs react strongest, suggesting that the "whisky interactome," i.e., the compounds or compound mixtures that are responsible for the generation of signal, are mostly negatively charged. Initial screenings with PAEs of diverse hydrophobicity and charge density show that a combination of both these interactions, but not either one alone, is required for creating distinct response patterns (Figure S32).

Principal-component analysis of the responses (for the details of the selection process, see Figure S11) selected three tongue elements (Figure 1) with the highest discriminative power: a positively charged PAE with a perfluorobenzylammonium group (**P1**) and two negatively charge PAEs (**P2** and **P3**), one carrying carboxylic acid groups and the other equipped with sulfonate groups.

[1]Organisch-Chemisches Institut, Ruprecht-Karls-Universität Heidelberg, Im Neuenheimer Feld 270

[2]Centre for Advanced Materials, Im Neuenheimer Feld 225

69120 Heidelberg, Germany

[3]Department of Polymer Chemistry and Bioengineering, Zernike Institute for Advanced Materials, University of Groningen, Nijenborgh 4, 9747 AG Groningen, the Netherlands

[4]Lead Contact

*Correspondence: a.herrmann@rug.nl (A.H.), uwe.bunz@oci.uni-heidelberg.de (U.H.F.B.)

http://dx.doi.org/10.1016/j.chempr.2017.04.008

Table 1. Tested Whiskies and Their Origin, Type, and Storage Age

Abbreviation	Whisky Brand	Origin	Type	Alcohol Content (% by Volume)	Storage Age (Years)
B-1	Jim Beam	bourbon whisky	bourbon	40	4
B-2	Jack Daniel's	bourbon whisky	bourbon	40	4
Ib-1	Jameson, John	Irish whiskey	blended	40	7
Ib-2	Kilbeggan	Irish whiskey	blended	40	NAS
Is-1	Kilbeggan	Irish whiskey	single malt	40	8
Is-2	Connemara	Irish whiskey	single malt	40	NAS
Is-3	Tyrconnell	Irish whiskey	single malt	40	NAS
Is-4	Tullamore Dew	Irish whiskey	single malt	40	NAS
Sb-1	MacNamara	Scotch whisky	blended	40	6
Sb-2	Ballantine's Finest	Scotch whisky	blended	40	NAS
Sb-3	Té Bheag Nan Eilean	Scotch whisky	blended	40	NAS
Sb-4	Dean's	Scotch whisky	blended	40	NAS
Sb-5	Grant's	Scotch whisky	blended	40	NAS
Sb-6	Johnnie Walker Red Label	Scotch whisky	blended	40	NAS
Sb-Y8[a]	Poit Dhubh	Scotch whisky	blended	43	8
Sb-Y12[a]	Poit Dhubh	Scotch whisky	blended	43	12
Sb-Y21[a]	Poit Dhubh	Scotch whisky	blended	43	21
Ss-1	Laphroaig Quarter Cask	Scotch whisky	single malt	48	7
Ss-2	Talisker Isle of Skye	Scotch whisky	single malt	46	10
Ss-3	Laphroaig	Scotch whisky	single malt	40	10
Ss-4	Cragganmore	Scotch whisky	single malt	40	12
Ss-5	Glenfiddich	Scotch whisky	single malt	40	12
Ss-6	GlenDronach	Scotch whisky	single malt	43	12
Ss-7	Glenfarclas	Scotch whisky	single malt	43	15
Ss-8	Dalwhinnie	Scotch whisky	single malt	43	15
Ss-9	Ardmore Legacy	Scotch whisky	single malt	40	NAS
Ss-10	Bowmore	Scotch whisky	single malt	40	NAS
Ss-11	Highland Park	Scotch whisky	single malt	40	12
Ss-12	Balvenie Double Wood	Scotch whisky	single malt	40	12
Ss-13	Glenlivet	Scotch whisky	single malt	43	18
Ss-Y12[a]	Bowmore	Scotch whisky	single malt	40	12
Ss-Y15[a]	Bowmore	Scotch whisky	single malt	43	15
Ss-Y18[a]	Bowmore	Scotch whisky	single malt	43	18
New-1	Ardbeg	Scotch whisky	single malt	46	10
New-2	Glenmorangie Original	Scotch whisky	single malt	40	10
Fake-1	Old Keeper	Scotch whisky	blended	40	NAS

Abbreviation: NAS, no age statement. See also Figures S1 and S2.

[a]The Y in the abbreviation of a whisky name means year.

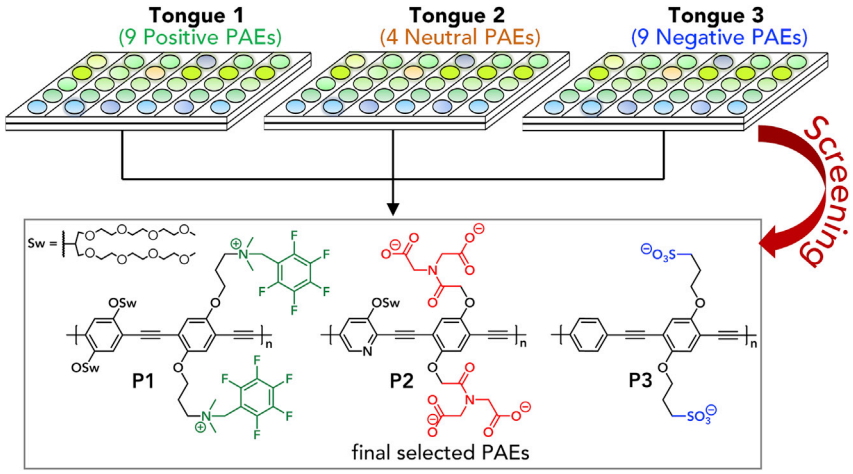


Figure 1. Screening of the PAE-Based Tongue

Selection of the three most discriminating elements for the formation of a functional sensor array (for the details of the selection process, see Figure S8).

Figure 2 depicts the overall results of the discrimination experiments. All of the whiskies were easily discriminated with the use of the data from the small conjugated polymer assay. The three factors suffice to uniquely discriminate all of the samples (the jackknifed classification matrix with cross-validation revealed 99% accuracy; Table S3 and Figure S16). Blind tests were performed with randomly chosen whiskies from our training set. The new cases were classified into groups generated from the

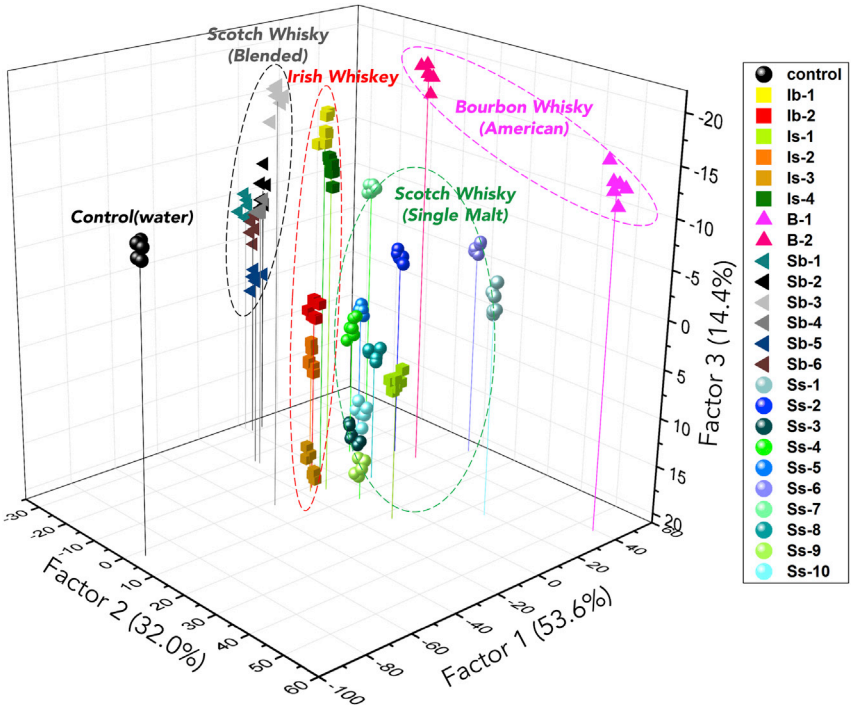


Figure 2. Discrimination of Whisky with the PAE-Based Tongue

3D LDA plot of the fluorescence modulation data obtained with an array of final selected PAEs treated with all of the whiskies investigated. Each point represents the response pattern for a single whisky to the array. The jackknifed classification matrix with cross-validation reveals 99% accuracy.

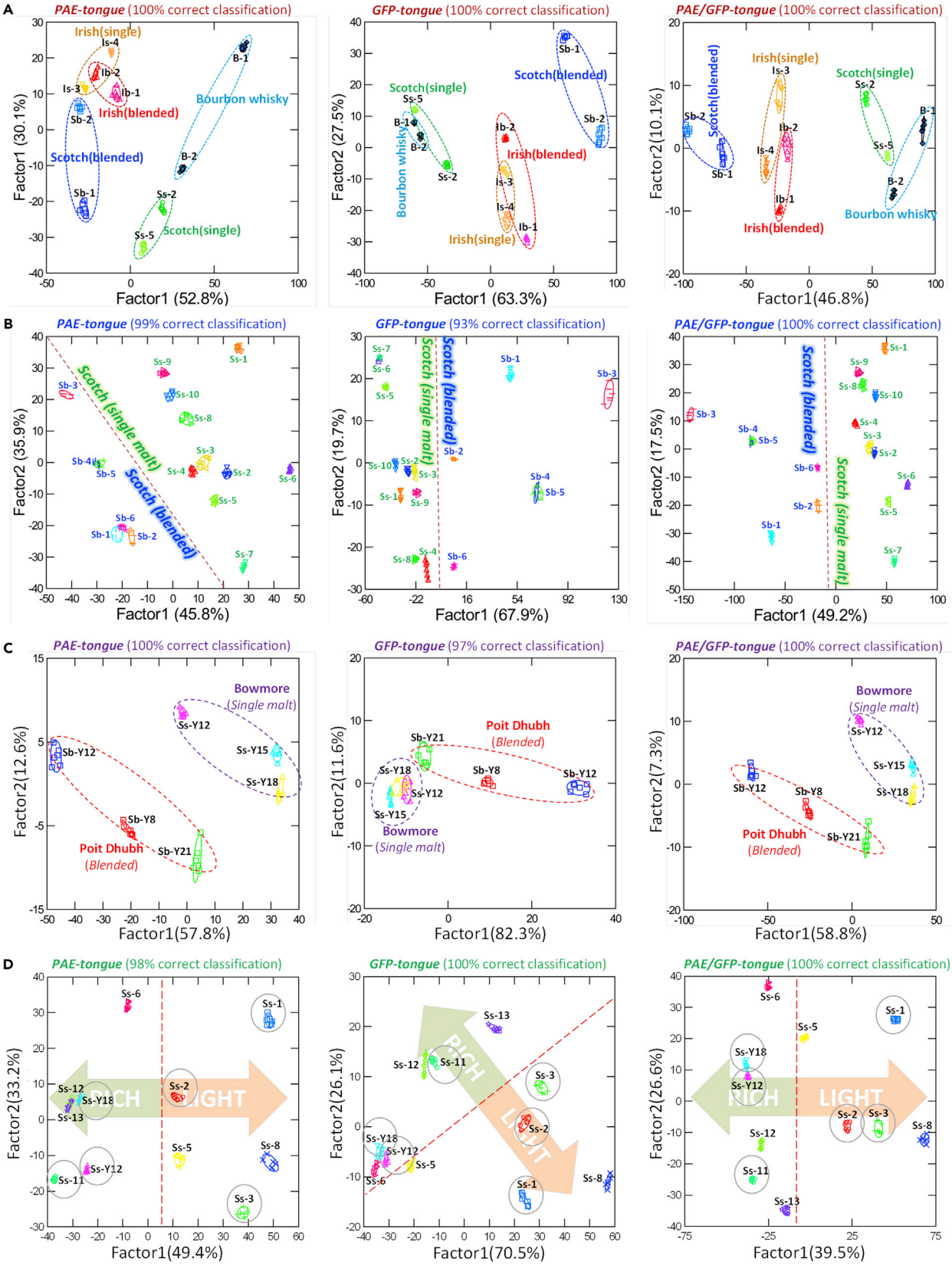

A
PAE-tongue (100% correct classification)
Factor1 (30.1%)
Factor1 (52.8%)
Irish(single)
Irish(blended)
Bourbon whisky
Scotch(blended)
Scotch(single)
GFP-tongue (100% correct classification)
Factor2 (27.5%)
Factor1 (63.3%)
Scotch(single)
Scotch(blended)
Bourbon whisky
Irish(blended)
Irish(single)
PAE/GFP-tongue (100% correct classification)
Factor2(10.1%)
Factor1(46.8%)
Scotch(blended)
Irish(single)
Scotch(single)
Irish(blended)
Bourbon whisky
B
PAE-tongue (99% correct classification)
Factor2 (35.9%)
Factor1 (45.8%)
Scotch (single malt)
Scotch (blended)
GFP-tongue (93% correct classification)
Factor2 (19.7%)
Factor1 (67.9%)
Scotch (single malt)
Scotch (blended)
PAE/GFP-tongue (100% correct classification)
Factor2 (17.5%)
Factor1 (49.2%)
Scotch (blended)
Scotch (single malt)
C
PAE-tongue (100% correct classification)
Factor2(12.6%)
Factor1(57.8%)
Bowmore
(Single malt)
Poit Dhubh
(Blended)
GFP-tongue (97% correct classification)
Factor2(11.6%)
Factor1(82.3%)
Poit Dhubh
(Blended)
Bowmore
(Single malt)
PAE/GFP-tongue (100% correct classification)
Factor2(7.3%)
Factor1(58.8%)
Bowmore
(Single malt)
Poit Dhubh
(Blended)
D
PAE-tongue (98% correct classification)
Factor2(33.2%)
Factor1(49.4%)
RICH
LIGHT
GFP-tongue (100% correct classification)
Factor2(26.1%)
Factor1(70.5%)
RICH
LIGHT
PAE/GFP-tongue (100% correct classification)
Factor2(26.6%)
Factor1(39.5%)
RICH
LIGHT

Figure 3. Discrimination of Whisky for Brand, Origin, Age, and Taste

Discrimination of the whiskies for (A) origin, (B) blending status, (C) age, and (D) taste for (left) a pure PAE tongue, (middle) a GFP-based tongue, and (right) a joint GFP-PAE tongue based on LDA with 95% confidence ellipses. The published richness-to-lightness gradation is **Ss-13**, **Ss-12**, **Ss-6**, **Ss-Y18**, **Ss-11**, **Ss-Y12**, **Ss-2**, **Ss-5**, **Ss-1**, **Ss-8**, and **Ss-3**.[24] The gray rings in the bottom row (D) denote whiskies that are labeled as smoky For details, see Tables S5–S16 and Figures S17–S28.

training matrix on the basis of the shortest Mahalanobis distance to the respective group. Four of 120 unknown whiskies were misclassified, representing an accuracy of 96.7% (see Table S4). To explore the reproducibility of our sensing system, we reproduced the 3D score plots from scratch by using a freshly made array of the PAE fluorophores (**P1–P3**); the results were almost superimposable (Figure S29). More interestingly, two new single malt Scotch whiskies (**New-1** and **New-2** in Table 1) were added and applied to our tongue. The fluorescence response was recorded and treated as a blind sample in the linear discriminant analysis (LDA) on the basis of the initial training set. As a result, the new whiskies (not part of the initial training set) were correctly identified as single malt Scotch whiskies (Figures S30 and S31). In the next step, the data from the LDA were analyzed with respect to specific properties (Figure 3; see also Tables S5–S16 and Figures S17–S28).

We discriminated different types of whiskies and distinguished between blended and single malt whiskies in all of the Scotch samples. We also investigated samples of whiskies of different ages. For Bowmore single malt, we found a linear relationship between age and response when looking at the LDA sub-plot (Figure 3C). In the blended whiskies, this relationship no longer held true. This is not too surprising because in blends, the ages of the constituent whiskies can and will vary to achieve a consistent taste and look. The last and perhaps most important quality is taste. Scotch is grouped along two different taste axes. The first axis is smoky and delicate and the second axis is light and rich.[24–26] Surprisingly, we cannot discriminate whiskies according to their peatiness, i.e., smoky character, but the array discriminates light from rich, very malty whiskies (Figure 3D).

Are PAEs the only fluorescent systems that discriminate whiskies? We investigated GFPs fused to unfolded supercharged polypeptide chains.[27,28] These genetically engineered tags consist mainly of the pentapeptide repeat $[GVGXP]_n$, where X is either a positively charged lysine (K) residue or a negatively charged glutamic acid (E).[29] These motifs were multimerized to exhibit 36 charged amino acids. The fluorescent protein tongue consisted of three elements: conventional GFP with a net charge of −7, a highly positively charged variant (GFP-K36), and a highly negatively charged variant (GFP-E36) (Figure 4; see also Table S1 and Figures S4–S6 and S9). The amount of whisky necessary for useful signal generation was lower than for the PAEs: 0.5 μL for GFP-K36, 1.5 μL for GFP, and 15 μL for GFP-E36 (for the details of the concentration and pH selection process, see Figure S12).

Figure 3 (middle) shows the overall sensing outcome for a GFP-based tongue. The results are consistent with those obtained by the PAE array. The analytes were not differentiated as well as with the PAEs, but considering that the direct protein environment close to the chromophore of GFP is very similar and structural differences are located at the rim of the folded scaffold, the results are remarkable. The positively charged GFP, similar to **P1**, reacted most sensitively to the whisky because its interactome must be negatively charged. A combined PAE-GFP tongue (Figure 3, right) was even better than each of the single tongues, particularly with respect to discriminating blends from single malt whiskies. It is surprising that two such chemically different tongues are supremely successful at differentiating whiskies.

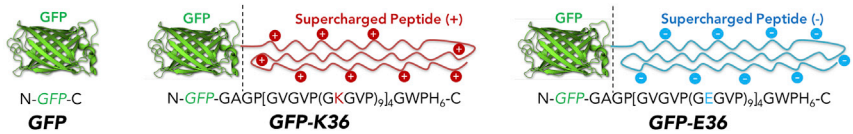


Figure 4. Construction of the GFP-Based Tongue
Different GFP variants used for sensing.

The arrays do not need any sample preparation; the analyte is pipetted to the solution of the fluorescent dyes. The analysis is performed with a standard plate reader on a 96-well plate. Multiple analytes are measured in one run, and data workup is performed by LDA with a commercial statistics software package. Alternative methods for investigating whiskies (e.g., mid-IR and simple UV-vis spectroscopy) either show a considerably lower resolving power with respect to the analytes or need a significant amount of sample preparation and fairly specialized equipment when performing mass spectrometry (MS) and gas chromatography mass spectrometry (GC-MS).[30] We performed an analysis of whiskies by using a standard GC-MS combination, but the results (see Table S2 and Figures S13–S15) were weaker than those for the tongues. We needed around 6 mL of sample and a significant amount of preparation time (for each sample, 30 min for liquid-liquid extraction and the mini silica gel column drying process and 30 min for GC-MS; for the details of the methods, procedures, and results, see Table S2 and Figures S13–S15). The relatively low resolution was disappointing. Although more specialized, electrospray-based MS approaches[31] do not need sample preparation and show improved discrimination, they still require a large investment in hardware and do not seem to quite reach the resolution that we obtained with simple fluorescence-based arrays.

DISCUSSION

In conclusion, two different, hypothesis-free, sensor arrays based upon three fluorophores each successfully discriminate whisky samples with respect to brand, origin, blending state, age, and taste. Both tongues create exquisitely sensitive patterns for whiskies on the basis of fluorescence modulation. Signal generation depends on fluorescence intensity modulation of the dyes; the nature of the excited state and its interaction with the analytes play critical roles. In conventional sensor applications, non-specific interactions are troublesome because they reduce fluorescence quantum yields and/or fluorescence lifetimes. Non-specific interactions exert undesired and unpredictable effects (Figure S32) that one can neither calculate nor model; however, when parallelized in sensor arrays, such interactions are the basis of discrimination and deliver spectacular power in hypothesis-free setups. Small sensor arrays based on charged fluorophore systems are powerful tools that discriminate any soluble analyte, apparently regardless of its structure, function, or origin.

EXPERIMENTAL PROCEDURES

Full experimental procedures are provided in the Supplemental Information.

SUPPLEMENTAL INFORMATION

Supplemental Information includes Supplemental Experimental Procedures, 32 figures, and 16 tables and can be found with this article online at http://dx.doi.org/10.1016/j.chempr.2017.04.008.

AUTHOR CONTRIBUTIONS

U.H.F.B., J.H., K.S., A.H., and M.B. conceived the experiments and the concepts. J.H., B.W., M.B., and M.H. prepared the polymers. C.M. and A.H. fabricated and

expressed the GFP variants. J.H. designed, screened, and developed the polymer tongue and performed the measurements. J.H., K.S., M.B., A.H., and U.H.F.B. analyzed and interpreted the experiments. U.H.F.B. and A.H. wrote the paper.

ACKNOWLEDGMENTS

J.H., C.M., and B.W. thank the China Scholarship Council for scholarships.

Received: February 28, 2017
Revised: March 21, 2017
Accepted: April 20, 2017
Published: June 8, 2017

REFERENCES AND NOTES

1. Wiskur, S.L., and Anslyn, E.V. (2001). Using a synthetic receptor to create an optical-sensing ensemble for a class of analytes: a colorimetric assay for the aging of scotch. J. Am. Chem. Soc. *123*, 10109–10110.

2. Wisniewska, P., Dymerski, T., Wardencki, W., and Namiesnik, J. (2015). Chemical composition analysis and authentication of whisky. J. Sci. Food Agric. *95*, 2159–2166.

3. Gonzalez-Arjona, D., Lopez-Perez, G., Gonzalez-Gallero, V., and Gonzalez, A.G. (2006). Supervised pattern recognition procedures for discrimination of whiskeys from gas chromatography/mass spectrometry congener analysis. J. Agric. Food Chem. *54*, 1982–1989.

4. Xu, M.L., Yu, Y., Ramaswamy, H.S., and Zhu, S.M. (2017). Characterization of Chinese liquor aroma components during aging process and liquor age discrimination using gas chromatography combined with multivariable statistics. Sci. Rep. *7*, 39671.

5. Mignani, A.G., Ciaccheri, L., Gordillo, B., Mencaglia, A.A., Gonzalez-Miret, M.L., Heredia, F.J., and Culshaw, B. (2012). Identifying the production region of single-malt scotch whiskies using optical spectroscopy and pattern recognition techniques. Sens. Actuators B Chem. *171*, 458–462.

6. Picque, D., Lieben, P., Corrieu, G., Cantagrel, R., Lablanquie, O., and Snakkers, G. (2006). Discrimination of cognacs and other distilled drinks by mid-infrared spectroscopy. J. Agric. Food Chem. *54*, 5220–5226.

7. Askim, J.R., Mahmoudi, M., and Suslick, K.S. (2013). Optical sensor arrays for chemical sensing: the optoelectronic nose. Chem. Soc. Rev. *42*, 8649–8682.

8. Suslick, K.S., Rakow, N.A., and Sen, A. (2004). Colorimetric sensor arrays for molecular recognition. Tetrahedron *60*, 11133–11138.

9. Lim, S.H., Feng, L., Kemling, J.W., Musto, C.J., and Suslick, K.S. (2009). An optoelectronic nose for the detection of toxic gases. Nat. Chem. *1*, 562–567.

10. Umali, A.P., and Anslyn, E.V. (2010). A general approach to differential sensing using synthetic molecular receptors. Curr. Opin. Chem. Biol. *14*, 685–692.

11. You, L., Zha, D.J., and Anslyn, E.V. (2015). Recent advances in supramolecular analytical chemistry using optical sensing. Chem. Rev. *115*, 7840–7892.

12. Wu, J.S., Kwon, B., Liu, W.M., Anslyn, E.V., Wang, P.F., and Kim, J.S. (2015). Chromogenic/fluorogenic ensemble chemosensing systems. Chem. Rev. *115*, 7893–7943.

13. Bunz, U.H., Seehafer, K., Bender, M., and Porz, M. (2015). Poly(aryleneethynylene)s (PAE) as paradigmatic sensor cores. Chem. Soc. Rev. *44*, 4322–4336.

14. Anzenbacher, P., Lubal, P., Bucek, P., Palacios, M.A., and Kozelkova, M.E. (2010). A practical approach to optical cross-reactive sensor arrays. Chem. Soc. Rev. *39*, 3954–3979.

15. Peveler, W.J., Yazdani, M., and Rotello, V.M. (2016). Selectivity and specificity: pros and cons in sensing. ACS Sens. *1*, 1282–1285.

16. Feng, X.L., Liu, L.B., Wang, S., and Zhu, D.B. (2010). Water-soluble fluorescent conjugated polymers and their interactions with biomacromolecules for sensitive biosensors. Chem. Soc. Rev. *39*, 2411–2419.

17. Liu, Y.L., and Bonizzoni, M. (2014). A supramolecular sensing array for qualitative and quantitative analysis of organophosphates in water. J. Am. Chem. Soc. *136*, 14223–14229.

18. De, M., Rana, S., Akpinar, H., Miranda, O.R., Arvizo, R.R., Bunz, U.H., and Rotello, V.M. (2009). Sensing of proteins in human serum using conjugates of nanoparticles and green fluorescent protein. Nat. Chem. *1*, 461–465.

19. Bunz, U.H., and Rotello, V.M. (2010). Gold nanoparticle-fluorophore complexes: sensitive and discerning "noses" for biosystems sensing. Angew. Chem. Int. Ed. *49*, 3268–3279.

20. Han, J., Bender, M., Seehafer, K., and Bunz, U.H. (2016). Identification of white wines by using two oppositely charged poly(p-phenyleneethynylene)s individually and in complex. Angew. Chem. Int. Ed. *55*, 7689–7692.

21. Han, J., Wang, B., Bender, M., Seehafer, K., and Bunz, U.H. (2017). Poly(p-phenyleneethynylene)-based tongues discriminate fruit juices. Analyst *142*, 537–543.

22. Han, J., Wang, B., Bender, M., Kushida, S., Seehafer, K., and Bunz, U.H. (2017). Poly(aryleneethynylene) tongue that identifies nonsteroidal anti-inflammatory drugs in water: a test case for combating counterfeit drugs. ACS Appl. Mater. Interfaces *9*, 790–797.

23. Miranda, O.R., You, C.C., Phillips, R., Kim, I.B., Ghosh, P.S., Bunz, U.H.F., and Rotello, V.M. (2007). Array-based sensing of proteins using conjugated polymers. J. Am. Chem. Soc. *129*, 9856–9857.

24. Wishart, D. (2009). The flavour of whisky. Significance *6*, 20–26.

25. Broom, D. (2014). The World Atlas of Whisky: More Than 200 Distilleries Explored and 750 Expressions Tasted (Octopus).

26. Wishart, D. (2006). Whisky Classified: Choosing Single Malts by Flavour (Pavilion).

27. Liu, K., Pesce, D., Ma, C., Tuchband, M., Shuai, M., Chen, D., Su, J.J., Liu, Q., Gerasimov, J.Y., Kolbe, A., et al. (2015). Solvent-free liquid crystals and liquids based on genetically engineered supercharged polypeptides with high elasticity. Adv. Mater. *27*, 2459–2465.

28. Pesce, D., Wu, Y.Z., Kolbe, A., Weil, T., and Herrmann, A. (2013). Enhancing cellular uptake of GFP via unfolded supercharged protein tags. Biomaterials *34*, 4360–4367.

29. Yang, H.G., Ma, C., Li, K.Y., Liu, K., Loznik, M., Teeuwen, R., van Hest, J.C.M., Zhou, X., Herrmann, A., and Wang, J.J. (2016). Tuning ice nucleation with supercharged polypeptides. Adv. Mater. *28*, 5008–5012.

30. Wisniewska, P., Sliwinska, M., Namiesnik, J., Wardencki, W., and Dymerski, T. (2016). The verification of the usefulness of electronic nose based on ultra-fast gas chromatography and four different chemometric methods for rapid analysis of spirit beverages. J. Anal. Methods Chem. *2016*, 8763436.

31. Moller, J.K.S., Catharino, R.R., and Eberlin, M.N. (2005). Electrospray ionization mass spectrometry fingerprinting of whisky: immediate proof of origin and authenticity. Analyst *130*, 890–897.